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Letter to the Editor

The article by Whittaker et al. [1] about long-lasting patent channels created by transmyocardial laser revascularization (TLR) brings up many questions. Why did a lower laser energy (5–6 mJ/pulse) lead to a more powerful healing reaction and, consequently, to a higher percentage of channels closed by scars than a higher laser energy (9–10 mJ/pulse)? Why were collagen fibers aligned perpendicular to the long axes of the closed channels? In Figure 3b of their article [1], cardiomyocytes are interspersed between and parallel to collagenous fibers on both sides of the obstructed channel. This finding suggests to me that the lower-energy laser beam was too weak to destroy the inner structure of the myocardium. As a result, only "channels" filled with irradiated tissue were formed. As is evidenced by the well-developed scar, these lesions provoked intense inflammation and healing in which injured and dying cardiomyocytes or their empty endomysial tubes served as a scaffold for the oriented deposition of collagenous fibers.

What was the mechanism leading to the formation of the patent channel in Figure 3a of Whittaker et al. [1]? It could not have been an immediate ablation of the myocardium, because the newly formed patent channel would have been flooded by blood, clotting immediately in contact with connective tissue. The clot would have induced its own organization by inflammation and healing, and the channel would have become obstructed by scar [2]. This sequence of events is a well-established medical paradigm incompatible with the authors' hypothesis of blood flowing from the ventricular cavity through laser channels to coronary vessels [1]. Such an interpretation must be supported by much better evidence than the presence of one pigment grain at the entry of one obstructed channel and two pigment grains in the subendothelial space (Fig. 2) [1].

The patent channels presented by Whittaker et al. [1] are similar to those obtained by Mack et al. [3]. Both channels were created by excimer laser and surrounded by inflammation and fibrosis. Mack et al. [3] believe that their channels were formed by myocardial ablation followed by channel obstruction by clotted blood and successive recanalization by angiogenesis. I propose that the channels presented by Mack et al. were not created by ablation but remained obstructed by irradiated cardiomyocytes, which underwent apoptosis in the end [4]. This hypothesis presumes that the cardiomyocytes obstructing the channels blocked their flooding by blood and provided time for intravascular hemostatic mechanisms to take place. As a result, the channels were not invaded by blood when irradiated cardiomyocytes underwent apoptosis and disappeared. It is plausible that the same mechanism took place in the formation of the patent channels reported by Whittaker et al. [1]. The fibrosis surrounding their patent channels may be explained by the influence of inevitable proinflammatory factors induced by TLR such as accidental cell death, secondary hemorrhage, high-protein edema, etc. [2,5].

By which mechanism did TLR protect the myocardium challenged by the left coronary artery occlusion [1] when the patent channels did not contain blood? In a small organ such as the rat heart, the creation of six transmural laser channels must have created a substantial injury, leading to inflammation, angiogenesis, and the development of collateral vessels [6]. This statement is supported by the low sizes (low energy, 53 ± 2%; high energy, 55 ± 4%) of the areas at risk in the rats used by the authors [1], whereas the areas at risk in normal rats of the same breed are about 70% [7, Fig. 6, top]. It is obvious that a reduction of the area at risk will lead to a decrease in the size of infarction.

Why have the hearts treated with high-pulse energy suffered from smaller infarctions than the hearts treated with low-pulse energy when the patent channels did not contain blood [1]? One possibility is that the opposite walls of patent channels slid repeatedly one against another during heart contractions, thereby inflicting additional injury on the myocardium. This mechanism would enhance angiogenesis and intensify the formation of collateral vessels between the left and

right coronary arteries [6]. Another possibility may result from the fact that the patent channels were filled with interstitial fluid. As such, they might have facilitated its movements between more and less oxygenated parts of the myocardium, contributing thereby to a more efficient supply and washout of cardiac metabolites [8].

There remain several topics to be clarified. Did the patent channels protect cardiomyocytes only in their vicinity or did they reduce the areas of necrosis without any particular influence on neighboring cardiomyocytes? I lacked a visual documentation of the most important statement, i.e., "Connections to the ventricular cavity were identified for all opened channels, and vessels were often seen connecting to the channels" [1]. The allegedly patent channel in Figure 1b of Whittaker et al. [1] perplexes me. Its entry, situated between two myocardial ridges (trabeculae carneae), is obstructed by scar and its continuation in the mid-myocardium is filled with yellow, i.e., muscular, tissue. Is this a consequence of a "donut type" [9] of laser beam power distribution?

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